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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
WINKLER, ULRIKE

ART UNIT	PAPER NUMBER
1648	25

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/380,015	KORTH ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *77-117* is/are pending in the application.

4a) Of the above claim(s) *87,96-107,110-112 and 114-117* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *77-86,88,89,108,109 and 113* is/are rejected.

7)☒ Claim(s) *90-95* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 April 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *21* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Amendment filed April 16, 2003 (Paper No. 23) in response to the Office Action of February 12, 2003 is acknowledged and has been entered. Claims 40-76 have been cancelled. Claims 77-86, 88-95, 108, 109 and 113 are pending and are currently being examined. Claims 87, 96-107, 110-112, 114-117 have been withdrawn as being drawn to non-elected subject matter of Paper No. 18.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Specification

The Office acknowledges the submission of an abstract.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, Paper No. 21, is attached to the instant Office action.

Drawings

The Office acknowledges the receipt of the corrected drawings. The drawings have been reviewed and approved by the draftsperson.

Claim Objections

The objections of claims 51-54, 67 and 68 **are withdrawn** in view of applicant' cancellation of the claims.

The objection of claim 40 **is withdrawn** in view of applicant's cancellation of the claims.

Claim Rejections - 35 USC § 102

The rejection of claims 40-49 and 72 under 35 U.S.C. 102(e) **is withdrawn** in view of the cancellation of the claims. However, the newly presented claims are rejected essentially for the same reason of record see below.

Rejection of newly presented claims:

Newly added claims 77-86, 88, 89, 108, 109 and 113 are rejected as being anticipated by Pruisiner et al. (U.S. Pat. No. 5,846,533) as evidenced by Billeter et al. (PNAS 1997).

Applicant arguments have been fully considered but fail to persuade. Applicant's arguments during the interview February 11, 2003 (Paper No. 20) and in the instant response April 16, 2003 (Paper No. 23) are based on a product-by-process analysis. Applicant's response is focused on the differences in the method used to obtain the antibodies, in the instant invention the method utilizes a mixture of reduced and oxidized recombinant prion protein which resembles the PrP^{C} and PrP^{Sc} structures of the protein found in nature for the immunization of prion knockout mice. Product-by-process claims are not limited to the manipulations of the recited steps, only to the structure implied by the steps. M.P.E.P. Section 2113. The instant

claims are drawn to monoclonal antibodies, which are products. Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure (monoclonal antibodies that recognize the disease form of the prion protein), the properties applicant discloses and/or claims are necessarily present. *In re Spada* 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Applicant further argues the use of the Billeter et al. reference as being a post filing date reference which as not being "art the time of the invention". Applicant's cite *Ciba Geigy Ccorp v. Alza* Corp 37 USPQ2d 1337, specifically the sentence "thus, although references cannot be combined for purposes of anticipation, additional references may be used to interpret the allegedly anticipating reference and shed light on what it would have meant to those skilled in the art at the time of the invention." The entire paragraph reads from *Ciba Geigy Ccorp v. Alza* Corp 37 USPQ2d 1337:

> "[E]xtrinsic evidence may be considered when it is used to explain, but not expand, the meaning of a reference." *In re Baxter Travenol Labs.* , 952 F.2d 388, 390, 21 USPQ2d 1281, 1284 (Fed. Cir. 1991) (citing *Scripps Clinic & Research Found. v. Genen-tech, Inc.*, 927 F.2d 1565, 1566-67, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991)). Thus, although references cannot be combined for purposes of anticipation, additional references may be used to interpret the allegedly anticipating reference and shed light on what it would have meant to those skilled in the art at the time of the invention. *Studiengesellschaft Kohle, m.b.H.v. Dart Indus., Inc.* , 726 F.2d 724, 726-27, 220 USPQ 841, 842 (Fed. Cir. 1984). However, "such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Continental Can Co. USA Inc. v. Monsanto Co.* , 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991).

It is the offices position that the structure of the prion protein is the same before or after the discovery the molecular model. Especially, since the reference was merely used to show that the epitopes which are currently claimed would be on the outside of the molecule and thereby

accessible to antibody binding, regardless of the method of how the antibody is made. Furthermore, the Office would like to draw applicant's attention to figure 2 (found within the four corner of the cited document), which was the only part of particular interest in the prior rejection. This figure is a reprint of an earlier publication and therefore the information contained within the figure was known to one of ordinary skill in the art "at the time of the invention".

To reiterate prior rejection, the instant invention is drawn to a monoclonal antibody or fragment thereof that is able to bind PrP^{Sc} (native disease specific prion protein) while not binding PrP^{C} (normal cellular prion protein). This antibody, will also bind at least one of sequences of SEQ ID NO 7-9 (note the claim does not require binding to all three sequences simultaneously). The instant inventions also contemplates monoclonal antibodies to prion proteins that bind SEQ ID Nos: 5 and 6. The monoclonal antibody will bind soluble, insoluble, oxidized or reduced prion protein. The antibody can be labeled so that it may be used for detection. Additionally, the monoclonal antibody will be used to formulate a pharmaceutical preparation.

Pruisiner et al. (U.S. Pat. No. 5,846,533) discloses monoclonal antibodies D4, R2, 6D2, D14, R1 and R10 (see column 38, lines 20-21). The antibodies are made by injecting a prion knockout mouse with purified prion rods (see column 28, line 15, to column 29, line 8; example 1 and claim 8). The antibody secreting B-cells are then isolated from spleen and these cells are used to create the phage display library (examples 4 and 5). The antibodies are obtained by panning the phage display library against PrP^{C}, only those phage that do not bind PrP^{C} were evaluated for their ability bind to PrP^{Sc} (see example 11, claim 1 and figures 9 and 10). As the

antibodies were screened the prion protein was either insoluble (ie. bound to the surface) or soluble when evaluating the ability of the monoclonal antibody to immunoprecipitation the prion protein. The reference also contemplates using the antibodies as a treatment (see column 10, lines6-27; column 21 lines 25-41). The antibodies can be used in immunoaffinity assays or coupled onto other surfaces (coupled to other molecules). The specific epitope bindings was not determined for the monoclonal antibodies disclosed, nor were the antibodies tested for their binding to recombinant, reduced or oxidized prion protein. The reference discloses antibodies (claim 3) that are able to bind cow, horse, dog, human, chicken and cat prions.

Antibody binding is dependent on the epitope structure, which is inherent to the amino acid sequence. Antibodies my bind linear epitopes or three-dimensional epitopes. The structure of a molecule is determined by the amino acid sequence, Billeter et al. (PNAS 1997, figure 2) shows the predicted NMR structure of a prion protein. Only epitopes that are located on the outside of a molecule would be accessible for antibody attachment. The epitopes disclosed in SEQ ID NO 5-9 are found on the outside of the prion molecule and therefore would accessible for antibody attachment. The epitopes are an inherent structural feature of the prion protein.

Applicant's arguments have addressed the different methodology used in preparing the instant monoclonal antibodies with the methods used in preparing the monoclonal antibodies from the prior art. The instantly claimed monoclonal antibodies and the prior art monoclonal antibodies bind to the same structure, i.e. the disease form of the prion protein. Because the PTO does not have laboratory facilities the PTO is not able to make structural assessments between the instantly claimed antibodies and the antibodies of the prior art. The arguments presented have not addressed the structural differences between the antibodies and have only addressed the

different methods of producing antibodies that recognize the same structure (the disease form of the prion protein). Therefore, applicants arguments are not persuasive in overcoming the rejection and the rejection is maintained.

Claims 90-95 are objected to because of the following informalities: The claims are dependent on rejected claims. Appropriate correction is required.

Claim 77 is objected to because of the following informalities: The claim utilizes an abbreviation PRP^C which is not disclosed in the specification, se page 2, which utilizes the abbreviation PrP^C. Because this is an obvious typographical error it is treated as an objection requiring appropriate correction rather that a written description rejection.

Allowable Subject Matter

The specific deposited antibody producing clones would be allowable DSM ACC2295 (34C9), DSM ACC2296 (6H4) and DSM ACC2298 (15B3) would be allowable.

Conclusion

Claims 77-86, 88, 89, 108, 109 and 113 are rejected.

Claims 90-95 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Ulrike Winkler, Ph.D.

JAMES HOUSEL 6/30/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600